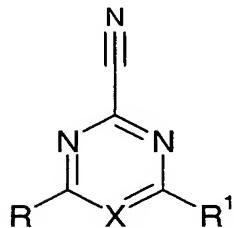


**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claim 1. (currently amended) A method of inhibiting cathepsin S in a mammal comprising administering use of a compound of formula (I) to said mammal



(I)

in which:

X is N or CA where A is hydrogen, halogen,  $\text{CHR}^2\text{R}^3$ ,  $\text{OR}^2$ ,  $\text{NR}^2\text{R}^3$ ,  $\text{SR}^2$ ;

$\text{R}^2$  and  $\text{R}^3$  are independently hydrogen,  $\text{C}_{1-6}$  alkyl or  $\text{C}_{3-6}$  cycloalkyl both of which can optionally contain one or more O, S or  $\text{NR}^4$  groups where  $\text{R}^4$  is hydrogen or  $\text{C}_{1-6}$  alkyl, and can be optionally substituted by aryl, heteroaryl,  $\text{NR}^5\text{R}^6$  where  $\text{R}^5$  and  $\text{R}^6$  together with the nitrogen atom to which they are attached form a 4-7 membered ring optionally containing a further O, S,  $\text{NR}^4$ , or R2 and R3 together with the nitrogen atom to which they are attached form a 4-7 membered ring optionally containing a further O, S,  $\text{NR}^4$  group, or R2 and R3 are aryl or heteroaryl groups, both aryl and heteroaryl groups being optionally substituted by halogen, amino, hydroxy, cyano, nitro, carboxy,  $\text{CONR}^7\text{R}^8$ ,  $\text{SO}_2\text{NR}^7\text{R}^8$ ,  $\text{SO}_2\text{R}^4$ , trifluoromethyl,  $\text{NHSO}_2\text{R}^4$ ,  $\text{NHCOR}^4$ , ethylenedioxy, methylenedioxy,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{1-6}$  alkoxy,  $\text{NR}^7\text{R}^8$  or  $\text{SR}^7$  where  $\text{R}^7$  and  $\text{R}^8$  are independently hydrogen or  $\text{C}_{1-6}$  alkyl;

R and R¹ are independently a group  $\text{Y}(\text{CH}_2)\text{pR}^9$  where p is 0, 1, 2 or 3 and Y is O or  $\text{NR}^{10}$  where  $\text{R}^{10}$  is hydrogen,  $\text{C}_{1-6}$  alkyl or  $\text{C}_{3-6}$  cycloalkyl;

and R<sup>9</sup> is hydrogen, C<sub>1-6</sub> alkyl which can optionally contain one or more O, S or NR<sup>4</sup> groups where R<sup>4</sup> is hydrogen or C<sub>1-6</sub> alkyl, or a 3 to 7-membered saturated ring optionally containing a carbonyl group, one or more O, S or N atoms, or an aryl or heteroaryl group containing one to four heteroatoms selected from O, S or N, the saturated ring, aryl and heteroaryl groups all being optionally substituted by halogen, amino, hydroxy, cyano, nitro, carboxy, CONR<sup>7</sup>R<sup>8</sup>, SO<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, SO<sub>2</sub>R<sup>4</sup>, trifluoromethyl, NHSO<sub>2</sub>R<sup>4</sup>, NHCOR<sup>4</sup>, ethylenedioxy, methylenedioxy, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, SR<sup>5</sup> or NR<sup>11</sup>R<sup>12</sup> where R<sup>11</sup> and R<sup>12</sup> are independently hydrogen, C<sub>1-6</sub> alkyl or together with the nitrogen atom to which they are attached form a 5- or 6-membered saturated ring optionally containing a further O, S or NR<sup>4</sup> group;  
 or R/R<sup>1</sup> is a group NR<sup>10</sup>(CHR<sup>10</sup>)CONR<sup>2</sup>R<sup>3</sup> or NR<sup>10</sup>(CH<sub>2</sub>)<sub>q</sub>CONR<sup>2</sup>R<sup>3</sup> where q is 1, 2 or 3;  
 or R/R<sup>1</sup> is a group NR<sup>13</sup>R<sup>14</sup> where R<sup>13</sup> and R<sup>14</sup> together with the nitrogen atom to which they are attached form a 4 to 7-membered saturated ring optionally containing a carbonyl group, O, S or N atom and optionally substituted by C<sub>1-6</sub> alkyl, amino, hydroxy, CO<sub>2</sub>C<sub>1-6</sub> alkyl, halogen, NR<sup>5</sup>R<sup>6</sup>, NR<sup>7</sup>R<sup>8</sup>, C<sub>1-6</sub> alkylNR<sup>17</sup>R<sup>18</sup> where R<sup>17</sup> and R<sup>18</sup> are independently hydrogen or C<sub>1-6</sub> alkyl, CONR<sup>15</sup>R<sup>16</sup> where R<sup>15</sup> and R<sup>16</sup> are independently hydrogen or C<sub>1-6</sub> alkyl, or optionally substituted by aryl, phenoxy, COphenyl, or a heteroaryl group, the latter four groups being optionally substituted by halogen, amino, hydroxy, cyano, nitro, carboxy, CONR<sup>7</sup>R<sup>8</sup>, SO<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, SO<sub>2</sub>R<sup>4</sup>, trifluoromethyl, NHSO<sub>2</sub>R<sup>4</sup>, NHCOR<sup>4</sup>, ethylenedioxy, methylenedioxy, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, SR<sup>5</sup> or NR<sup>11</sup>R<sup>12</sup> where R<sup>11</sup> and R<sup>12</sup> are independently hydrogen, C<sub>1-6</sub> alkyl or together with the nitrogen atom to which they are attached form a 5- or 6-membered saturated ring optionally containing a further O, S or NR<sup>4</sup> group;

and pharmaceutically acceptable salts or solvates thereof, in the manufacture of a medicament for use in the inhibition of cathepsin S in a mammal such as man.

Claim 2. (currently amended) ~~Use compound~~The method according to claim 1 in which X is CH, NHR<sup>2</sup>, OR<sup>2</sup> wherein R<sup>2</sup> is hydrogen or C<sub>1-6</sub> alkyl.

Claim 3. (currently amended) ~~Use compound~~The method according to claim 1 or 2 in which R is a group Y(CH<sub>2</sub>)<sub>p</sub>R<sup>7</sup> where p is 0 or 1 and Y is NR<sup>8</sup> wherein R<sup>8</sup> is hydrogen and R<sup>7</sup> is substituted phenyl.

Claim 4. (currently amended) ~~Use compound~~The method according to any one of claims 1 to 3 in which R<sup>1</sup> is a group NR<sup>13</sup>R<sup>14</sup> where R<sup>13</sup> and R<sup>14</sup> together with the nitrogen atom to which they are attached form a morpholine ring, piperidine or piperazine ring optionally substituted.

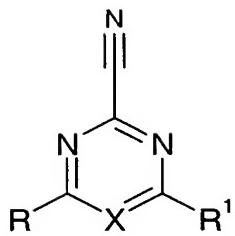
Claim 5. (currently amended) Use compound The method according to any one of claim 1s-1 to 3-in which R<sup>1</sup> is a group NR<sup>9</sup>R<sup>10</sup> where R<sup>10</sup> is H or C<sub>1-6</sub> alkyl and R<sup>9</sup> is C<sub>1-6</sub> alkyl which can optionally contain one or more O, S or NR<sup>4</sup> groups where R<sup>4</sup> is hydrogen or C<sub>1-6</sub> alkyl.

Claim 6.(currently amended) Use The method according to claim 1 where the compound of formula (I) is selected from:

4-[(4-Chlorophenyl)amino]-6-(dimethylamino)-1,3,5-triazine-2-carbonitrile,  
 4-Morpholin-4-yl-6-(4-phenoxyperidin-1-yl)-1,3,5-triazine-2-carbonitrile,  
 4-[(4-Chlorophenyl)amino]-6-morpholin-4-yl-1,3,5-triazine-2-carbonitrile,  
 4-(7-Azabicyclo[2.2.1]hept-7-yl)-6-[(4-chlorophenyl)amino]-1,3,5-triazine-2-carbonitrile,  
 4-[(4-Chlorophenyl)amino]-6-pyrrolidin-1-yl-1,3,5-triazine-2-carbonitrile,  
 4-[(4-Chlorophenyl)amino]-6-piperidin-1-yl-1,3,5-triazine-2-carbonitrile,  
 4-[(4-Chlorophenyl)amino]-6-(ethylamino)-1,3,5-triazine-2-carbonitrile,  
 4-[(4-Chlorophenyl)amino]-6-(3-hydroxypyrrolidin-1-yl)-1,3,5-triazine-2-carbonitrile,  
 4-[(4-Chlorophenyl)amino]-6-[(2-piperidin-1-ylethyl)amino]-1,3,5-triazine-2-carbonitrile,  
 4-[(4-Chlorophenyl)amino]-6-(4-phenylpiperidin-1-yl)-1,3,5-triazine-2-carbonitrile,  
 4-[(3-Chlorobenzyl)amino]-6-(dimethylamino)-1,3,5-triazine-2-carbonitrile,  
 4-Morpholin-4-yl-6-[(4-morpholin-4-ylphenyl)amino]-1,3,5-triazine-2-carbonitrile,  
 4-(2,3-Dihydro-1,4-benzodioxin-6-ylamino)-6-morpholin-4-yl-1,3,5-triazine-2-carbonitrile,  
 4-Morpholin-4-yl-6-(3-phenylpiperidin-1-yl)-1,3,5-triazine-2-carbonitrile,  
 4-(1,4'-Bipiperidin-1'-yl)-6-morpholin-4-yl-1,3,5-triazine-2-carbonitrile,  
 4-[4-(1H-Imidazol-1-yl)piperidin-1-yl]-6-morpholin-4-yl-1,3,5-triazine-2-carbonitrile,  
 4-[4-(4-Chlorobenzoyl)piperidin-1-yl]-6-morpholin-4-yl-1,3,5-triazine-2-carbonitrile,  
 4-[4-(5-Chloropyridin-2-yl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazine-2-carbonitrile,  
 4-Morpholin-4-yl-6-{[3-(2-oxopyrrolidin-1-yl)propyl]amino}-1,3,5-triazine-2-carbonitrile,  
 1-(4-Cyano-6-morpholin-4-yl-1,3,5-triazin-2-yl)-N,N-diethylpiperidine-3-carboxamide,  
 4-[4-(2-Methoxyphenyl)piperazin-1-yl]-6-morpholin-4-yl-1,3,5-triazine-2-carbonitrile,  
 N~2~~(4-Cyano-6-morpholin-4-yl-1,3,5-triazin-2-yl)-N~1~,N~1~~bis{4-[N-(4-cyano-6-morpholin-4-yl-1,3,5-triazin-2-yl)-N-isobutylglycyl]morpholin-3-yl}-N~2~~isobutylglycinamide,  
 4-Morpholin-4-yl-6-[(2-pyridin-3-ylethyl)amino]-1,3,5-triazine-2-carbonitrile,  
 4-{[2-(2-Furyl)ethyl]amino}-6-morpholin-4-yl-1,3,5-triazine-2-carbonitrile,  
 4-[(4-Chlorophenyl)amino]-6-(4-methylpiperazin-1-yl)-1,3,5-triazine-2-carbonitrile,  
 4-Azetidin-1-yl-6-[(4-chlorophenyl)amino]-1,3,5-triazine-2-carbonitrile,  
 4-[(4-Chlorophenyl)amino]-6-morpholin-4-ylpyrimidine-2-carbonitrile,  
 4-[(4-Methylcyclohexyl)amino]-6-morpholin-4-ylpyrimidine-2-carbonitrile,  
 4-(4-Chlorophenoxy)-6-morpholin-4-ylpyrimidine-2-carbonitrile,

4-[(4-Chlorophenyl)amino]-6-(dimethylamino)pyrimidine-2-carbonitrile,  
4-[(1-Methylpiperidin-4-yl)amino]-6-morpholin-4-ylpyrimidine-2-carbonitrile,  
4-(Cyclohexylamino)-6-morpholin-4-ylpyrimidine-2-carbonitrile,  
4-[(4-Chlorophenyl)amino]-6-pyrrolidin-1-ylpyrimidine-2-carbonitrile,  
4-[(6-Chloropyridin-3-yl)amino]-6-morpholin-4-ylpyrimidine-2-carbonitrile,  
1-{6-[(4-Chlorophenyl)amino]-2-cyanopyrimidin-4-yl}-L-prolinamide,  
4-(4-Aminopiperidin-1-yl)-6-[(4-chlorophenyl)amino]pyrimidine-2-carbonitrile,  
4-[(4-Chlorophenyl)amino]-6-(4-pyrrolidin-1-ylpiperidin-1-yl)pyrimidine-2-carbonitrile,  
4-[(4-Chlorophenyl)amino]-6-[(3-pyrrolidin-1-ylpropyl)amino]pyrimidine-2-carbonitrile,  
tert-Butyl 4-{6-[(4-chlorophenyl)amino]-2-cyanopyrimidin-4-yl}piperazine-1-carboxylate,  
4-[(4-Chlorophenyl)amino]-6-(cyclopropylamino)pyrimidine-2-carbonitrile,  
4-[(4-Chlorophenyl)amino]-6-piperazin-1-ylpyrimidine-2-carbonitrile,  
(2S)-N~2~-{6-[(4-Chlorophenyl)amino]-2-cyanopyrimidin-4-yl}-N~1~,N~1~-bis[4-(N-{6-  
[(4-chlorophenyl)amino]-2-cyanopyrimidin-4-yl}-L-leucyl)morpholin-3-yl]-L-leucinamide,  
5-Chloro-4-[(4-chlorophenyl)amino]-6-morpholin-4-ylpyrimidine-2-carbonitrile,  
4-[(4-Chlorophenyl)amino]-5-methoxy-6-piperazin-1-ylpyrimidine-2-carbonitrile,  
4-[(4-Chlorophenyl)amino]-5-methoxy-6-morpholin-4-ylpyrimidine-2-carbonitrile,  
4-[(3S)-3-Aminopyrrolidin-1-yl]-6-[(4-chlorophenyl)amino]-5-methoxypyrimidine-2-  
carbonitrile,  
4-[(4-Chlorophenyl)amino]-6-{4-[3-(dimethylamino)propyl]piperazin-1-yl}-5-  
methoxypyrimidine-2-carbonitrile,  
4-[(4-Chlorophenyl)amino]-6-(dimethylamino)-5-methoxypyrimidine-2-carbonitrile,  
4-[(4-Chlorophenyl)amino]-5-methoxy-6-(3-oxopiperazin-1-yl)pyrimidine-2-carbonitrile,  
1-{6-[(4-Chlorophenyl)amino]-2-cyano-5-methoxypyrimidin-4-yl}piperidine-3-carboxamide,  
4-(4-Aminopiperidin-1-yl)-6-[(4-chlorophenyl)amino]-5-methoxypyrimidine-2-carbonitrile,  
5-Amino-4-[(4-chlorophenyl)amino]-6-morpholin-4-ylpyrimidine-2-carbonitrile,  
5-Amino-4-[(4-Chlorophenyl)amino]-6-(ethylamino)pyrimidine-2-carbonitrile,  
and pharmaceutically acceptable salts thereof.

Claim 7. (currently amended) A compound of formula (I):



(I)

in which:

$\text{X}$  is CA where A is hydrogen, halogen,  $\text{CHR}^2\text{R}^3$ ,  $\text{OR}^2$ ,  $\text{NR}^2\text{R}^3$ ,  $\text{SR}^2$ ;

$\text{R}^2$  and  $\text{R}^3$  are independently hydrogen,  $\text{C}_{1-6}$  alkyl or  $\text{C}_{3-6}$  cycloalkyl both of which can optionally contain one or more O, S or  $\text{NR}^4$  groups where  $\text{R}^4$  is hydrogen or  $\text{C}_{1-6}$  alkyl, and can be optionally substituted by aryl, heteroaryl,  $\text{NR}^5\text{R}^6$  where  $\text{R}^5$  and  $\text{R}^6$  together with the nitrogen atom to which they are attached form a 4-7 membered ring optionally containing a further O, S,  $\text{NR}^4$ , or R2 and R3 together with the nitrogen atom to which they are attached form a 4-7 membered ring optionally containing a further O, S,  $\text{NR}^4$  group, or R2 and R3 are aryl or heteroaryl groups, both aryl and heteroaryl groups being optionally substituted by halogen, amino, hydroxy, cyano, nitro, carboxy,  $\text{CONR}^7\text{R}^8$ ,  $\text{SO}_2\text{NR}^7\text{R}^8$ ,  $\text{SO}_2\text{R}^4$ , trifluoromethyl,  $\text{NHSO}_2\text{R}^4$ ,  $\text{NHCOR}^4$ , ethylenedioxy, methylenedioxy,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{1-6}$  alkoxy,  $\text{NR}^7\text{R}^8$  or  $\text{SR}^7$  where  $\text{R}^7$  and  $\text{R}^8$  are independently hydrogen or  $\text{C}_{1-6}$  alkyl;

$\text{R}$  and  $\text{R}^1$  are independently a group  $\text{Y}(\text{CH}_2)\text{pR}^9$  where  $\text{p}$  is 0, 1, 2 or 3 and  $\text{Y}$  is O or  $\text{NR}^{10}$  where  $\text{R}^{10}$  is hydrogen,  $\text{C}_{1-6}$  alkyl or  $\text{C}_{3-6}$  cycloalkyl; and  $\text{R}^9$  is hydrogen,  $\text{C}_{1-6}$  alkyl which can optionally contain one or more O, S or  $\text{NR}^4$  groups where  $\text{R}^4$  is hydrogen or  $\text{C}_{1-6}$  alkyl, or a 3 to 7-membered saturated ring optionally containing a carbonyl group, one or more O, S or N atoms, or an aryl or heteroaryl group containing one to four heteroatoms selected from O, S or N, the saturated ring, aryl and heteroaryl groups all being optionally substituted by halogen, amino, hydroxy, cyano, nitro, carboxy,  $\text{CONR}^7\text{R}^8$ ,  $\text{SO}_2\text{NR}^7\text{R}^8$ ,  $\text{SO}_2\text{R}^4$ , trifluoromethyl,  $\text{NHSO}_2\text{R}^4$ ,  $\text{NHCOR}^4$ , ethylenedioxy, methylenedioxy,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{1-6}$  alkoxy,  $\text{SR}^5$  or  $\text{NR}^{11}\text{R}^{12}$  where  $\text{R}^{11}$  and  $\text{R}^{12}$  are independently hydrogen,  $\text{C}_{1-6}$  alkyl or together with the nitrogen atom to which they are attached form a 5- or 6-membered saturated ring optionally containing a further O, S or  $\text{NR}^4$  group; or  $\text{R/R}^1$  is a group  $\text{NR}^{10}(\text{CHR}^{10})\text{CONR}^2\text{R}^3$  or  $\text{NR}^{10}(\text{CH}_2)_q\text{CONR}^2\text{R}^3$  where  $q$  is 1, 2 or 3;

or R/R<sup>1</sup> is a group NR<sup>13</sup>R<sup>14</sup> where R<sup>13</sup> and R<sup>14</sup> together with the nitrogen atom to which they are attached form a 4 to 7-membered saturated ring optionally containing a carbonyl group, O, S or N atom and optionally substituted by C<sub>1-6</sub> alkyl, amino, hydroxy, CO<sub>2</sub>C<sub>1-6</sub> alkyl, halogen, NR<sup>5</sup>R<sup>6</sup>, NR<sup>7</sup>R<sup>8</sup>, C<sub>1-6</sub> alkylNR<sup>17</sup>R<sup>18</sup> where R<sup>17</sup> and R<sup>18</sup> are independently hydrogen or C<sub>1-6</sub> alkyl, CONR<sup>15</sup>R<sup>16</sup> where R<sup>15</sup> and R<sup>16</sup> are independently hydrogen or C<sub>1-6</sub> alkyl, or optionally substituted by aryl, phenoxy, COphenyl, or a heteroaryl group, the latter four groups being optionally substituted by halogen, amino, hydroxy, cyano, nitro, carboxy, CONR<sup>7</sup>R<sup>8</sup>, SO<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, SO<sub>2</sub>R<sup>4</sup>, trifluoromethyl, NHSO<sub>2</sub>R<sup>4</sup>, NHCOR<sup>4</sup>, ethylenedioxy, methylenedioxy, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, SR<sup>5</sup> or NR<sup>11</sup>R<sup>12</sup> where R<sup>11</sup> and R<sup>12</sup> are independently hydrogen, C<sub>1-6</sub> alkyl or together with the nitrogen atom to which they are attached form a 5- or 6-membered saturated ring optionally containing a further O, S or NR<sup>4</sup> group;

or and pharmaceutically acceptable salts or solvates thereof..

Claim 8. (cancelled).

Claim 9. (original) A pharmaceutical composition which comprises a compound of the formula (I) as defined in claim 7 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable diluent or carrier.

Claim 10. (original) A method for producing inhibition of a cysteine protease in a mammal, such as man, in need of such treatment, which comprises administering to said mammal an effective amount of a compound of the present invention as defined in claim 7 or a pharmaceutically acceptable salt thereof.